Research Highlight

Exercise in type 2 diabetes: The mechanisms of resistance and endurance training

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This highlight article focuses on the effects of different types of exercise on the prevention and treatment of type 2 diabetes and on future challenges in developing effective preventive strategies.

1. Current prevalence of diabetes in China

Cardiovascular diseases have become the leading cause of death in China.1 Diabetes is a major risk factor for cardiovascular diseases and the rapid change in lifestyle is the main reason for the increased risk for cardiovascular diseases in China.1–3 The China National Diabetes and Metabolic Disorders Study,3 consisting of a nationally representative sample of 46,239 adults, found that age-standardized prevalence of diabetes was 10.6% among men and 8.8% among women, and for prediabetes the figures were 16.1% and 14.9% for men and women, respectively. This corresponds to 92.4 million adults with diabetes and 148.2 million adults with prediabetes. Clearly diabetes has become a huge public health challenge in China and developing effective preventive strategies for diabetes is therefore essential.3

2. Endurance (aerobic) and strength (resistance) exercise training in the prevention and treatment of type 2 diabetes

The first randomized controlled trial including an exercise only arm in the prevention of diabetes was conducted in China from 1986 to 1992, and the results suggested that increased aerobic exercise has an independent role in the prevention of type 2 diabetes after 6 years of intervention.4 Since the pioneering study by Eriksson et al.5 it has been known that, in addition to aerobic training, strength training is also beneficial for type 2 diabetes patients. A randomized controlled study by Sigal et al.6 showed that both aerobic training and resistance training alone improve glycemic control in patients with type 2 diabetes, and the improvement after 22 weeks of exercise training seems to be greater with combined, rather than they are applied in isolation. A recent study conducted by van Dijk et al.7 concluded that a single session of resistance- or endurance-type exercise reduces the prevalence of hyperglycaemia and improves glycaemic control during the subsequent 24 h period in individuals with impaired glucose tolerance, and in insulin-treated and non-insulin-treated type 2 diabetic patients. Despite these short-term and relatively long-term randomized controlled trials, it is still not well known whether increased volume or combination of training modalities is more important than exercise type. Furthermore, the mechanistic differences between the two training modalities in improving glycemic control are unclear.8

Skeletal muscles typically represent more than one-third of body mass and play an important role in whole-body energy metabolism. During exercise, work is mainly done by skeletal muscles and this work is mediated by various signaling pathways. At the cellular level, exercise increases insulin-dependent glucose transport and hexokinase II activity.9 Furthermore, muscular contraction induces an increase in translocation of glucose transporter type 4 through AMP-activated protein kinase signaling pathways during endurance exercise training in the acute phase.10,11 After exercising, increased adenosine triphosphate synthesis and, later, increased mitochondrial biogenesis via activation of peroxisome-proliferator activated receptor-γ coactivator 1α, increases muscle insulin sensitivity in the post-exercise...
period.\textsuperscript{12} Another proposed mechanism is increased membrane permeability accompanied by elevated insulin-stimulated microvascular perfusion in the post-exercise state which could favor glucose uptake.\textsuperscript{12}

The cellular mechanisms of acute resistance-type exercise are less clear. An increase in muscle mass over time has been thought to account for the benefits of resistance exercise on glycemic control and the associated expansion of glucose disposal capacity.\textsuperscript{13} The study by van Dijk et al.\textsuperscript{7} showed that a single bout of resistance exercise reduced the prevalence of hyperglycaemia by about 36\% during the 24-h post-exercise period. The authors ascribed these acute improvements in glycemic control following resistance exercise to direct improvements in insulin-dependent and insulin-independent glucose uptake, similar to the effects generally observed after endurance exercise. However, it remains to be established whether resistance exercise can also modulate glycemic control throughout subsequent day/s, and whether the acute glucose regulatory effects of resistance exercise remain at lower intensities.\textsuperscript{7} More studies are needed to determine whether strength or endurance type training should be recommended to improve glycemic control.

The effects of training on skeletal muscle and glucose metabolism may be also modulated by variants in genes. A recent study conducted by Barres et al.\textsuperscript{14} showed that acute aerobic exercise alters global and gene-specific promoter methylation in skeletal muscle suggesting that DNA hypomethylation is an early event in contraction-induced gene activation. Further, they found that exercise-induced effects on DNA methylation are dependent on exercise intensity. These findings provide further evidence that the epigenetic marks across the genome are subject to more dynamic variations than previously appreciated.\textsuperscript{14}

3. Future challenges

Both in-depth mechanistic studies and long-term trials are needed to clarify the overall long-term effects of different types of training on disease progression, occurrence of related cardio-vascular diseases, complications and mortality. One of the novel mechanisms needing further study is microRNAs and their regulation in the context of insulin resistance.\textsuperscript{15} Furthermore, adipose tissue has an important role as an energy store and dysregulation of its function also predicts cardio-metabolic diseases. Recently, the importance and interaction of muscle and adipose tissues for disease risk has received much attention.\textsuperscript{16} The large-scale potential of exercise training probably lies in its ability to induce many health benefits at the same time leading to better fitness and function in later years.\textsuperscript{17} Our understanding of genetics, the effects of exercise and their interactions is accumulating rapidly. In addition to clarifying these relationships using different modern approaches there is a continuous need to carry out large-scale long-term randomized controlled trials to explore the effects of exercise. Differences in the determinants and potential to respond to exercise training by age need more study. Overall, a life-long physically active lifestyle seems to bestow the highest health benefits. Consequently, long-term adherence to exercise advice rather than specific modes of exercise might ultimately determine efficacy to improve glycaemia and the associated morbidity and mortality.

References